

REMARKS

Status Summary

Claims 1 and 3-46 are presently pending in the instant U.S. Patent Application. The U.S. Patent and Trademark Office (hereinafter the "Patent Office") has issued a Final Official Action. Claims 1 and 3-46 presently stand rejected.

Claims 1, 4, 6, 7, 19, 20, 25-28 and 42 stand rejected by the Patent Office under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by PCT International Patent Application Publication No. WO98/44910 to Lang (hereinafter "Lang").

Claims 8, 12, 13, 15-18, 22, 23, 29-31, 33, 34 and 46 are rejected under 35 U.S.C. 103(a) upon the contention that the claims are unpatentable over Lang in view of U.S. Patent No. 5,810,888 to Fenn (hereinafter "Fenn").

Claims 3, 9-11, 35 and 37-40 are rejected under 35 U.S.C. 103(a) upon the contention that the claims are unpatentable over Lang in view of Fenn and further in view of U.S. Patent No. 5,149,319 to Unger (hereinafter "Unger '319").

Claims 14, 24, 32, 36, 41 and 43-45 are rejected under 35 U.S.C. 103(a) upon the contention that the claims are unpatentable over Lang in view of Fenn, further in view of Unger '319 and further in view of U.S. Patent No. 5,542,935 to Unger et al. (hereinafter "Unger et al. '935").

Claims 5 and 21 are rejected under 35 U.S.C. 103(a) upon the contention that the claims are unpatentable over Lang in view of U.S. Patent No. 4,728,575 to Gamble et al. (hereinafter "Gamble et al.").

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Claims 1, 3-7 and 35 have been canceled without prejudice. Claims 8, 11, 19, 29, 36-39 and 42-44 have been amended to more particularly point out and distinctly claim the presently disclosed subject matter. Support for the amendments can be found throughout the application as filed, and particularly at page 6, line 30, through page 7, line 3; page 32, lines 24-32; and page 36, lines 16-26. No new matter has been added.

New claim 47 has been added. Support for new claim 47 can be found throughout the specification as originally filed and particularly at page 38, lines 9-13. No new matter has been added.

Reconsideration of the application as amended and based on the remarks set forth below is respectfully requested.

Response to the Rejection of Claims Under 35 U.S.C. § 102(b)

Based on Lang

Claims 1, 4, 6, 7, 19, 20, 25-28 and 42 stand rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Lang. The Patent Office asserts that Lang discloses a method comprising identical active steps of the subject invention as claimed. More specifically, the Patent Office asserts that Lang discloses a method of monitoring drug delivery to a tumor, comprising administering a non-sensitive liposome composition, wherein the liposome encapsulates a contrast agent and a therapeutic agent, and monitoring the accumulation of the compound of interest at the tumor site using MRI.

The positions of the Patent Office as summarized above with respect to claims 1, 4, 6, 7, 19, 20, 25-28 and 42 are respectfully traversed as described below.

Applicants respectfully submit that claims 1, 4, 6 and 7 have been canceled, thus mooted the instant rejection as it pertains to these claims.

Furthermore, claim 19 has been amended to recite, *inter alia*, "A method of detecting an *in vivo* blood pool, the method comprising: (i) a contrast agent; and (ii) a liposome encapsulating the contrast agent, wherein the liposome composition has the ability to remain in the subject's blood stream for a protracted period of time without being recognized by the subject's reticuloendothelial system...". Support for the amendment to claim 19 can be found throughout the specification as originally filed and particularly at page 36, lines 16-26. No new matter has been added.

Applicants respectfully submit that Lang does not teach or suggest a liposome composition having the ability to remain in the subject's blood stream for a protracted period of time without being recognized by the reticuloendothelial system. Therefore, applicants respectfully submit that Lang does not support a rejection of claim 19 under 35 U.S.C. § 102(b).

Because claims 20 and 25-28 depend from claim 19 and therefore share the novel features of claim 19 described above, applicants respectfully submit that claims 20 and 25-28 are also patentably distinguished over Lang. Accordingly, the rejection of claims 19, 20 and 25-28 under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Lang is believed to have been addressed. Allowance of the claims is respectfully requested.

As for claim 42, applicants respectfully submit that this claim recites, *inter alia*, "monitoring in real time the accumulation of the compound of interest at a desired site by magnetic resonance imaging." By the Patent Office's own admission, Lang does not teach monitoring of the compound in real time. See, e.g., page 8 of the Official Action. Therefore, applicants respectfully submit that Lang does not support a rejection of claim 42 under 35 U.S.C. § 102(b).

Thus, applicants respectfully submit that claims 19, 20, 25-28 and 42 are patentably distinguished over Lang. Withdrawal of the rejection of claims 19, 20, 25-28 and 42 under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Lang is respectfully requested. Allowance of claims 19, 20, 25-28 and 42 is also respectfully requested.

Response to the Rejection of Claims Under 35 U.S.C. § 103(a)

Based on Lang in View of Fenn

Claims 8, 12, 13, 15-18, 22, 23, 29-31, 33, 34 and 46 stand rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Lang in view of Fenn. As described above, the Patent Office asserts that Lang discloses a method of monitoring drug delivery to a tumor, comprising administering a non-sensitive liposome composition, wherein the liposome encapsulates a contrast agent and a therapeutic agent, and monitoring the accumulation of the compound of interest at the tumor site by MRI. The Patent Office admits that the reference lacks

particular disclosure about the use of a thermosensitive liposome. However, the Patent Office contends that the teachings of the Fenn compensate for this deficiency.

According to the contentions of the Patent Office, Fenn teaches the use of a thermosensitive liposome for drug delivery by transmitting electromagnetic radiation to the site of interest wherein the liposome contains chemotherapy agents. The Patent Office also contends that Fenn discloses the possibility of using medical imaging modalities such as MRI to detect the temperature of the site while heating. Therefore, the Patent Office contends that it would have been *prima facie* obvious to one of ordinary skill in the art to modify Lang to include the use of a thermosensitive liposome in the method of drug delivery and monitoring as evidenced by Fenn.

The positions of the Patent Office as summarized above with respect to claims 8, 12, 13, 15-18, 22, 23, 29-31, 33, 34 and 46 are respectfully traversed as described below.

Applicants respectfully submit that the aforementioned discussion regarding the deficiencies of the methods disclosed by Lang with respect to present claim 19 is maintained in response to the current rejection. Applicants respectfully submit that claims 22 and 23 depend from claim 19. Applicants respectfully submit that Fenn does not compensate for the deficiencies of Lang. Accordingly, applicants respectfully submit that the instant rejection with respect to claims 22 and 23 has been addressed.

Additionally, applicants respectfully submit that claims 8 and 29 have been amended to clarify the claimed methods. In particular, applicants respectfully submit that claim 8 has been amended to recite, *inter alia*, “An *in vivo* method of monitoring the localization and distribution of a compound of interest to a desired site in an organism by magnetic resonance imaging, the method comprising: (a) administering an envirosensitive liposome composition to a subject...; and (b) monitoring the localization and distribution of the compound of interest to a desired site by magnetic resonance imaging, wherein the monitoring comprises monitoring the release of the contents of the liposome by monitoring an increase in the presence of contrast agent as the contents of the liposome are being released”. Claim 29, directed to a method of monitoring the accumulation of a compound of interest at a desired site *in vivo*, has been amended in a similar manner. Support for the amendments to claims 8 and 29 can be found throughout the specification as originally filed, and particularly at page 32, lines 24-32. No new matter has been added.

Applicants respectfully submit that neither Lang nor Fenn, alone or in combination, teach or suggest methods of monitoring the localization and distribution (claim 8), or accumulation (claim 29), of a compound of interest to a desired site, wherein the monitoring comprises monitoring the release of the contents of the liposome by monitoring an increase in the presence of contrast agent as the contents of the liposome are being released. Stated another way, the proposed combination of Lang and Fenn does not teach or suggest a method of monitoring drug distribution or accumulation wherein the release of the drug from the liposome is verified.

The Patent Office contends that Lang teaches the monitoring of the compound of interest via MRI and that Fenn teaches the release of a compound of interest at a desired site. However, applicants respectfully submit that Fenn merely assumes that the contents of the liposomes were released, and provides no data, other than some unsupported conclusory statements, to support the notion that the contents were indeed released from the liposomes.

As discussed in the specification, delivering drugs to a specific target *in vivo* using envirosensitive liposomes is dependent upon the ability to effectively release the drug from the liposome at the desired target upon the selective application of an environmental factor. At the time of filing of the instant patent application this was problematic. In particular, page p. 4, line 8, through page 5, lines 7, of the specification states the following:

Liposome targeting, however, depends in part on how stably the liposomes administered to a subject circulate through the circulatory system in the normal physiological environment and how effectively the liposomes release their content (e.g. a drug) at a particular desired site (e.g. a tumor). In the case of some thermosensitive liposomes targeting has been problematic. For example, the liposomes described by Yatvin et al. (Yatvin et al., (1978) *Science* 202: 1290) release only a small amount of the drug at the temperature of hyperthermia. Other liposomes have been observed to release the drug at a temperature lower (e.g., 37-39°C.) than that typically reached in an approach employing hyperthermia (Bassett et al., (1986) *J. Urol.* 135(3): 612-615; Needham et al., (2000) *Cancer Res.* 60(5): 1197-1201).

However, an approach for monitoring the release of liposome contents once an envirosensitive liposome has lost structural integrity has not been disclosed in the art. Therefore, absent a method of monitoring liposome opening and content release, a clinician or researcher must assume that the liposome was delivered to the desired site, that it ruptured and released its contents and that the contents were delivered to the desired site.

Thus, what is needed is an envirosensitive liposome, for example a thermosensitive liposome composition that exhibits a desirable phase transition at the typical temperature of hyperthermia (40-45°C), or a radiation sensitive liposome that exhibits a desirable phase transition when contacted by a particular wavelength range of electromagnetic radiation. Further, what is needed is an envirosensitive liposome that is adapted to entrap a drug at a high concentration for long periods of time when maintained at physiological conditions, for example a temperature lower than that of hyperthermia for thermosensitive liposomes, and that is adapted to release the drug efficiently in a very short time after a particular environmental stimulation, for example at the temperature of hyperthermia or higher for thermosensitive liposomes. Such an envirosensitive liposome composition would also be adapted to be tracked to a desired location, wherein content delivery could be monitored *in vivo* by a non-invasive method.

(emphasis added).

Therefore, even assuming *arguendo* the one of ordinary skill in the art would have combined the teachings of Lang and Fenn, applicants respectfully submit that the proposed combination does not teach each and every element of the claims, particularly tracking the release of the contents of the liposome by monitoring an increase in the presence of contrast agent. Therefore, applicants respectfully submit that the proposed combination of Lang and Fenn does not support a rejection of claims 8 and 29 under 35 U.S.C. § 103(a).

Continuing with the instant rejection, applicants respectfully submit that the proposed combination of Lang and Fenn does not teach or suggest an *in vivo* method of monitoring the localization and distribution or the accumulation of a compound of interest, wherein the monitoring is performed as the contents of the liposome are being released from the envirosensitive liposome at the desired site.

As discussed in the previously filed Official Action response (Amendment A, April 23, 2007), the monitoring of the accumulating or localization and distribution of the compound of interest can be accomplished in less than five minutes (see, for example, page 42, lines 24-30) and as little as 1 minute 45 seconds (see, for example, page 49, lines 18-19).

In response, the Patent Office states that Lang in combination with Fenn clearly teaches monitoring release of a compound of interest as it is released from the liposome since Lang allegedly teaches monitoring the compound via MRI and Fenn allegedly teaches releasing the compound of interest with focused radiation. However, applicants again contend that the methods disclosed by Lang require substantially longer time periods for the monitoring disclosed therein. For example, tumor enhancement 5 minutes after Gd-labeled liposomes were injected provided only minimal enhancement of tumor tissue and tumor tissue enhancement, not believed to be statistically different from a pre-contrast image, and did not reach a maximum until 24 hours post injection. See page 12, lines 10-20, and Figure 1, of Lang. Accordingly, pre- and postcontrast images would be obtained with a time separation of 24 hours and thus could not be done within a single imaging session. See page 18, lines 3-5, of Lang. As such, the monitoring in Lang is not analogous to the monitoring in the presently disclosed and claimed subject matter. Additionally, Fenn does not compensate for this deficiency in Lang, as Fenn only assumes that the contents of the liposomes were released and makes no mention of an ability to monitor the release.

Therefore, applicants respectfully submit that it would not have been *prima facie* obvious to a skilled artisan at the time of the invention to combine the teachings of Lang and Fenn to provide a method of monitoring the localization and distribution or accumulation of a compound of interest in accordance with the presently claimed subject matter. Further, there would have been no reasonable expectation of success in combining the teachings of Lang and Fenn to provide methods in accordance with the presently claimed subject matter.

Thus, applicants respectfully submit that present claims 8 and 29 are believed to be distinguished from the proposed combination of Lang and Fenn. As claims 12, 13, 15-18, 30-31, 33, 34 and 46 depend either directly or indirectly from claims 8 and 29 they too are believed to be distinguished from the proposed combination of Lang and Fenn.

Accordingly, applicants respectfully request withdrawal of the rejection of claims 8, 12, 13, 15-18, 22, 23, 29-31, 33, 34 and 46 under 35 U.S.C. § 103(a). A Notice of Allowance is also respectfully requested.

Response to the Rejection of Claims Under 35 U.S.C. § 103(a)

Based on Lang in View of Fenn and Further in View of Unger '319

Claims 3, 9-11, 35 and 37-40 stand rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Lang in view of Fenn and further in view of Unger '319. As described above, the Patent Office asserts that Lang discloses a method of monitoring drug delivery to a tumor, comprising administering

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a non-sensitive liposome composition, wherein the liposome encapsulates a contrast agent and a therapeutic agent, and monitoring the accumulation of the compound of interest at the tumor site by MRI. Further, the Patent Office contends that Fenn teaches the use of a thermosensitive liposome. The Patent Office admits that neither Lang nor Fenn, alone or in combination, teaches the use of ultrasound to heat the tumor site. However, the Patent Office contends that the teachings of Unger '319 compensate for this deficiency.

According to the contentions of the Patent Office, Unger '319 teaches the use of ultrasound to heat the tumor site. Therefore, the Patent Office contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of Unger '319 with that of Lang.

The positions of the Patent Office as summarized above with respect to claims 3, 9-11, 35 and 37-40 are respectfully traversed as described below.

Applicants respectfully submit that claim 3 has been canceled, thus mooted the instant rejection as it pertains to this claim.

Applicants respectfully submit that the aforementioned discussion regarding the deficiencies of the methods disclosed by Lang and Fenn in monitoring the accumulation and distribution of a compound of interest *in vivo* is maintained in response to the current rejection.

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Applicants respectfully submit that Unger '319 does not compensate for the deficiencies of Lang and/or Fenn. Rather, Unger '319 at best teaches a method of heat treating biological tissues and fluids using a hyperthermic potentiator in combination with ultrasound. In particular, applicants respectfully submit that Unger '319 does not disclose a method of monitoring the localization and distribution of a compound of interest at a desired site, wherein the monitoring comprises monitoring the release of the contents of the liposome by monitoring an increase in the presence of the contrast agent as the contents of the liposome are being released, as recited in present claim 8, from which claims 9-11 depend, and therefore does not compensate for the deficiencies of Lang and/or Fenn.

With respect to claims 35 and 37-40, applicants respectfully submit that claim 35 has been canceled thereby mooted the instant rejection with respect to this claim. Furthermore, claims 37-40 have been amended to depend from claim 45. Claim 45 recites, *inter alia*, "generating in real time a heating profile of the site of interest.". By the Patent Office's own admission, the proposed combination of Lang, Fenn and Unger '319 does not teach monitoring of the compound in real time. See, e.g., page 8 of the Official Action. Therefore, applicants respectfully submit that the proposed combination of Lang, Fenn and Unger '319 does not support a rejection of present claims 37-40 under 35 U.S.C. § 103(a).

Thus, applicants respectfully request that the rejection of claims 9-11 and 37-40 under 35 U.S.C. 103(a) be withdrawn. Applicants also respectfully request that the claims be allowed.

Response to the Rejection of Claims Under 35 U.S.C. § 103(a) Based on Lang in View of Fenn, Further in View of Unger '319 and Further in View of Unger et al. '935

Claims 14, 24, 32, 36, 41 and 43-45 stand rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Lang in view of Fenn, further in view of Unger '319 and further in view of Unger et al. '935. As described above, the Patent Office asserts that Lang discloses a method of monitoring drug delivery to a tumor, comprising administering a non-sensitive liposome composition, wherein the liposome encapsulates a contrast agent and a therapeutic agent, and monitoring the accumulation of the compound of interest at the tumor site by MRI. Further, the Patent Office contends that Fenn teaches the use of a thermosensitive liposome and Unger '319 teaches the use of ultrasound to heat the tumor site. The Patent Office admits that none of these references described disclose a particular formulation of a thermo-sensitive liposome. However, the Patent Office contends that Unger et al. '935 compensates for this deficiency by disclosing many different formulations of liposomes.

According to the contentions of the Patent Office Unger et al. '935 discloses many different formulations of liposomes, including DPPC-PEG. Therefore, the Patent Office contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use a thermosensitive liposome comprising a formulation of PEG and DPPC.

The positions of the Patent Office as summarized above with respect to claims 14, 24, 32, 36, 41 and 43-45 are respectfully traversed as described below.

Applicants respectfully submit that claim 41 has been canceled, thus mooted the instant rejection as it pertains to this claim.

Applicants respectfully submit that the aforementioned discussion regarding the deficiencies of the methods disclosed by Lang, Fenn and Unger '319 are maintained in response to the current rejection.

Accordingly, applicants respectfully submit that Unger et al. '935 does not compensate for the above-noted deficiencies in Lang, Fenn and Unger '319. In particular, Unger et al. '935 does not disclose a method of monitoring the localization and distribution (claim 8) or accumulation (claim 29) of a compound of interest at a desired site, wherein the monitoring comprises monitoring the release of the contents of the liposome by monitoring an increase in the presence of the contrast agent as the contents of the liposome are being released, as recited in present claims 8 and 29, from which claims 14 and 32 depend, respectively, and therefore does not compensate for the deficiencies of the proposed combination of Lang, Fenn and Unger '319.

Claim 44 has been amended in a manner similar to that of claims 8 and 29. As with claims 8 and 29, no new matter is believed to have been added. As such, applicants respectfully submit that claim 44 is believed to be distinguished from the proposed combination of Lang, Fenn, Unger '319 and Unger et al. '935 for at least the reasons discussed hereinabove.

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Additionally, applicants respectfully submit that Unger et al. '935 does not compensate for the above-noted deficiencies in Lang, Fenn and Unger '319 with respect to present claim 19. In particular, Unger et al. '935 does not teach a liposome composition having the ability to remain in the subject's blood stream for a protracted period of time without being recognized by the subject's reticuloendothelial system, as recited in present claim 19. Claim 24 depends from claim 19 and therefore shares the novel features of claim 19.

Claim 43 has been amended in a manner similar to that of claim 9. As with claim 19, no new matter is believed to have been added. As such, applicants respectfully submit that claim 43 is believed to be distinguished from the proposed combination of Lang, Fenn, Unger '319 and Unger et al. '935 for at least the reasons discussed hereinabove.

Regarding claim 45, applicants respectfully submit that the claimed method recites *inter alia* real time generation of a heating profile. The Patent Office admits that the combination of Lang, Fenn and Unger '319 does not teach or suggest the ability to conduct the methods in real time, but contends that Unger et al. '935 compensates for this deficiency. The Patent Office contends that "by monitoring the release of the [of] contrast agent, a temperature will be inherently reached by the thermosensitive liposome which would serve to release the contrast agent." See, page 8 of the Official Action.

In response, applicants respectfully submit that it is not clear how the above noted statement in the Official Action regarding claim 45 establishes a *prima facie* case of obviousness. It is not clear how the Patent Office's statement regarding claim 45 is relevant to the real time generation of a heating profile. Further, the Patent Office has not directed applicant's attention to the specific portion of Unger et al. '935 that compensates for the admitted deficiencies in Lang, Fenn and Unger '319 with respect to generating a heating profile in real time, as recited in claim 45. As such, applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case of obviousness of claim 45 over the proposed combination of Lang, Fenn, Unger '319 and Unger et al. '935.

Furthermore, regarding claim 45, as well as claims 42-44, which all recite a real time element, applicants respectfully submit that Unger et al. '935 does not compensate for the deficiencies noted hereinabove with respect to Lang. In particular and as noted above, the imaging described in Lang requires pre- and postcontrast images obtained with a time separation of 24 hours. See page 18, lines 3-5, of Lang. This type of monitoring is clearly not analogous to the real time monitoring of the presently disclosed and claimed subject matter. The Patent Office refers to column [35] 36, lines 6-25 of Unger et al. '935, and contends that the disclosure therein compensates for the deficiencies of Lang. However, applicants respectfully disagree. The mere mention of "real time" in Unger et al. '935 does not cure this deficiency in Lang, as the method of Lang still requires monitoring over a 24-hour period.

Claim 36 has been amended to depend from claim 45, and is therefore believed to be patentable for at least the reasons discussed above.

Thus, applicants respectfully submit that Unger et al. '935 does not compensate for the deficiencies of the proposed cited combination. Applicants respectfully request that the rejection of claims 14, 24, 32, 36 and 45 under 35 U.S.C. 103(a) be withdrawn. Applicants also respectfully request that the claims be allowed.

Response to the Rejection of Claims Under 35 U.S.C. § 103(a)

Based on Lang in view of Gamble et al.

Claims 5 and 21 stand rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Lang in view of Gamble et al. As described above, the Patent Office asserts that Lang discloses a method of monitoring drug delivery to a tumor, comprising administering a non-sensitive liposome composition, wherein the liposome encapsulates a contrast agent and a therapeutic agent, and monitoring the accumulation of the compound of interest at the tumor site by MRI. The Patent Office admits that the reference lacks particular disclosure about the use of a liposome wherein the liposome DSPC/Cholesterol. However, the Patent Office contends that the teachings of the Gamble et al. compensate for this deficiency.

According to the contentions of the Patent Office Gamble et al. teach the use of a liposome comprising DSPC/Cholesterol. Therefore, the Patent Office contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the

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time the claimed invention was made to combine the teachings of Gamble et al. with that of Lang.

The positions of the Patent Office as summarized above with respect to claims 5 and 21 are respectfully traversed as described below.

Applicants respectfully submit that claim 5 has been canceled, thus mooted the instant rejection as it pertains to this claim.

Applicants respectfully submit that the aforementioned discussion regarding the deficiencies of the methods disclosed by Lang with respect to present claim 19 is maintained in response to the current rejection. Applicants respectfully submit that claim 21 depends from claim 19. Applicants respectfully submit that Gamble et al. does not compensate for the deficiencies of Lang. Accordingly, applicants respectfully submit that the instant rejection with respect to claim 21 has been addressed.

Thus applicants respectfully submit that Gamble et al. does not compensate for the deficiencies of Lang. Applicants respectfully request that the rejection of claim 21 under 35 U.S.C. 103(a) be withdrawn. Applicants also respectfully request that the claim be allowed.

DISCUSSION OF NEW CLAIM

New claim 47 has been added. New claim 47 depends from claim 19. Support for new claim 47 can be found throughout the specification as originally filed and particularly at page 38, lines 9-13. No new matter has been added.

The subject matter of claim 47 is not believed to be disclosed in any of the prior art documents of record. Accordingly, claim 47 is believed to be patentable for at least the reasons discussed hereinabove. Allowance of claim 47 is therefore respectfully requested.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

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DEPOSIT ACCOUNT

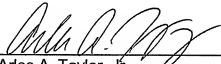
The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. 50-0426.

Respectfully submitted,

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